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10/813,506	03/29/2004	Daniel D. Shoemaker	9301-235-999	5273
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JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			EXAMINER STAPLES, MARK	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/813,506	Applicant(s) SHOEMAKER ET AL.	
	Examiner Mark Staples	Art Unit 1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 February 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 122, 178 and 185-232 is/are pending in the application.
- 4a) Of the above claim(s) 178, 186-188, 190, 191, 193-196, 198-199, 201-220, 225, and 227 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 122, 185, 189, 192, 197, 200, 221-224, 226 and 228-232 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Correction and Re-Issue of Final Action*

1. This is a correction and re-issue of the prior Final Office Action mailed on 05/15/2007. Applicant timely notified the Office of an error in not indicating the basis for rejection of amended claim 185. This action is in reply to Applicant's Response filed on 02/14/2007 after the non-final rejection. The time period for reply to this present action is 3 months.

2. Applicants' amendment of claims 122, 178, 185-188, 190-216, 218-220, 225-228, and 232 the paper filed on 02/14/2007 is acknowledged.

It is noted that claim 205 is listed as previously presented, when in fact this claim has been amended, appropriate correction is required.

Claims 178, 186-188, 190, 191, 193-196, 198, 199, 201-219, 225, and 227 were previously withdrawn and remain withdrawn as non-elected, see Office Action mailed on 11/14/2006.

Claim 220 is withdrawn as being dependent on withdrawn claim 217.

Claims 122, 185, 189, 192, 197, 200, 221-224, 226, and 228-232 are pending and at issue.

3. Applicants' arguments filed on 02/14/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied.

Art Unit: 1637

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Objections and Rejections that are Withdrawn**

***Objections to Specification Withdrawn***

4. The objection to the abstract is withdrawn in light of the Applicant's amendment of the abstract.
5. The objection to the title is withdrawn in light of the Applicant's amendment of the title.
6. The objection to the specification is withdrawn in light of the Applicant's amendment of the specification to refer to SEQ ID NO: 1.
7. The objection to the improper use of trademark CY DYE™ in the specification is withdrawn in light of Applicant's amendment for proper use of the trademark CY DYE™.

***Objections to Specification Withdrawn***

8. The objection to claims 228-231 is withdrawn in light of the Applicant's amendment of these claims.

***Claim Rejections Withdrawn - 35 USC § 112 Second Paragraph***

Art Unit: 1637

9. The rejections of claims 122, 185, 189, 192, 197, 200, 221-224, 226, and 228-232 under 35 USC § 112 Second Paragraph are withdrawn in light of Applicant's amendments to these claims.

***Claim Rejections Withdrawn - 35 USC § 112 First Paragraph***

10. The rejections of claims 185, 189, 192, 197, 200, 221-224, 226, and 228-232 under 35 USC § 112 First Paragraph are withdrawn in light of Applicant's amendment clarifying claim 185 and thus subsequent dependent claims.

***Rejections that are Maintained***

***Claim Rejections Maintained - 35 USC § 103***

***The Present Rejections / The Law Of Obviousness***

11. In response to applicant's argument on pages 16-18 that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

***The Presently Claimed Invention***

***Lockhart / Bowtell***

12. The rejection of claims 122, 189, 192, 197, 200, 221-222, 224, 226, and 228-232 under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. in view of Bowtell is maintained.

Applicant's arguments filed 02/14/2007 have been fully considered but they are not persuasive.

Applicant argues that the rejections do not properly address the following two points: (1) the distance between the 5' ends of the sequential sites is always less than 500 bp reflecting the density of the genomic sequences and (2) the genomic sequences span a genomic region of least 25,000 reflecting the span of the genomic sequences. Applicant places emphasis on both of these being claimed limitations of the instant invention. The rejections made in the prior Office Action mailed on 11/14/2006 include both of these limitations in the combined teachings of Lockhart and Bowtell.

On pages 19-20, Applicant presents no answerable argument regarding that Lockhart et al. does teach the *high density* of the claimed invention. Thus it is concluded that the high density teaching of Lockhart et al. is established. Applicant does argue that Lockhart et al. does not teach the *long span* of the claimed invention, but Bowtell is the source relied upon for this teaching. Also Applicant does admit that Lockhart et al. does in fact use sequences less than 500 bp (see 1<sup>st</sup> paragraph on p. 20) rendering contention on this point moot. The distance between sequential sites was always less than 500 bp.

On pages 21-22, Applicant presents no answerable argument regarding that Bowtell does teach the *long span* of the claimed invention. Thus it is concluded that the *long span* teaching of Bowtell is established. Applicant does argue that Bowtell does not teach the *high density* of the claimed invention, but Lockhart is the source relied upon for this teaching.

Applicant further argues there is no motivation to combine the teachings of Lockhart et al. and Bowtell. In response to this argument of Applicant, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Bowtell provides the motivation to combine the long genome span with high density of Lockhart et al. Bowtell states many benefits of spanning a genome throughout his teaching. For example, Bowtell states: "Obtaining the entire genomic sequence of *S. cerevisiae* allowed a near-complete set of genes to be generated by PCR, which have been arrayed and analysed<sup>7</sup>" (p. 29, 2<sup>nd</sup> sentence of 1<sup>st</sup> paragraph). Bowtell provides further motivation by describing the goals of the art at the time of the claimed invention: "The use of DNA microarrays for comprehensive RNA expression analysis has caused a great deal of interest recently, although the concept is not new<sup>1,2</sup>. Technical developments that offer increased sensitivity, the prospect that ***all genes*** for a given organism could soon be scrutinized in this way and a general appreciation of

Art Unit: 1637

the need to integrate information obtained from more traditional and reductionist approaches to biology make microarray-based expression analysis a powerful tool<sup>3</sup>" (p. 25, first two sentences, emphasis by Examiner). Thus from the teachings of Bowtell one of ordinary skill in the art would have been highly motivated to use the high density array as taught by Lockhart et al. to span a genome.

### ***Schena***

13. The rejection of claim 223 under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. and Bowtell and further in view of Schena et al. is maintained.

Applicant's arguments filed 02/14/2007 have been fully considered but they are not persuasive.

Applicant argues that Schena et al. does not provide motivation to combine long span and high density. However, it is the teachings of Bowtell, as noted above, which provide this motivation. Schena et al. teaches the use of microarrays to measure plant gene expression, thus rendering obvious the limitation of claim 223. Applicant does not counter this teaching by argument and thus the rejection of claim 223 is maintained.

All prior art rejections are maintained. Claim rejections are presented below.



**Rejections Maintained and Necessitated by Amendment**

14. Claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226, and 228-232 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (US Patent No. 6,329,140 filed 1997), cited on the Information Disclosure Statement (IDS) and Bowtell (1999).

Regarding claims 122 and 200, Lockhart et al. teach an array, comprising:  
a positionally-addressable ordered array of polynucleotide probe s bound to a solid support (entire reference especially Figures 1-4 and column 23 line 28-29: "Probes may be laid out on an polynucleotide array with a specifically defined positional relationship");

and said polynucleotide probes comprising a plurality of at least 100 polynucleotide probes of different nucleotide sequences (entire reference especially Figures 1-4 and claim 1 "at least four hundred different polynucleotides sequences per square centimeter"), each said different nucleotide sequence comprising a sequence complementary and hybridizable to a different genomic sequence of the same species of organism, said different genomic sequences being found at sequential sites in the genome of said species of organism (entire reference, especially Figure 2, Brief Description of the Figures, and SEQ ID NOS: 6-37 for the specie Homo Sapiens), wherein the distance between 5' ends of said sequential sites is always less than 500 bp (entire reference, especially "Single Increment Tiling" found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature includes nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30 , 25 or 15

Art Unit: 1637

nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 300 or less, the distance between 5' ends of any two sequential overlapping sites always must be less than 500 bp; as the maximum 5' distance end to end, which needs to include at least 1 overlapping nucleotide, is  $300-1 = 299$  bp; the minimum for this example being  $15-1 = 14$  bp).

Regarding claim 185, Lockhart et al. teach that a desired level of information may be determined, that is, that one can exclude low information content (see column 12 lines 7-10). As the specification does not provide a closed definition of "low information", this teaching of Lockhart et al. reads on the claim language. This is a rejection necessitated by amendment.

Regarding claim 189, Lockhart et al. teach an array with probe density ranging from 625 to 10 million probes per  $1\text{ cm}^2$  and thus teach an array having greater than 50,000 different polynucleotide probes per  $1\text{ cm}^2$ . (col. 7, lines 1-9).

Claim 192 is interpreted as reciting an array where the genomic sequences targeted by the probes are spaced apart by less than 200 bp. Lockhart et al. teach an array where the sequences targeted by the probes are spaced apart by less than 200 bp (entire reference, especially "*Single Increment Tiling*" found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature include nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30, 25 or 15 nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 200 or less, the distance between 5' ends of any two sequential overlapping sites

Art Unit: 1637

always must be less than 200 bp; as the maximum 5' distance end to end, which needs to include at least 1 overlapping nucleotide, is  $200-1 = 199$  bp).

Claim 197 is interpreted as reciting an array wherein each nucleotide sequence in the array consists of 10-200 nucleotides. Regarding claim 197, Lockhart et al. teach an array wherein each nucleotide sequence of the array consist of 102-103 nucleotide sequences as given in SEQ ID NOS: 5-37 (See Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claims 221, 222 and 224, Lockhart et al. teach wherein the organism is a human, *Homo Sapiens*, which is a mammal which is an eukaryote (see Sequence Listing for SEQ ID NOS: 5-27 where the organism is *Homo Sapiens*, Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claim 226, Lockhart et al. teach an array with at least 10,000 probes by teaching high density arrays, with probe density ranging from 625 to 10 million probes per  $1\text{ cm}^2$ . (Fig. 2; col. 6, lines 62-67; col. 7).

Claims 228-231 are interpreted as reciting an array in contact with a sample containing cellular RNA or nucleic acid under conditions conducive to hybridization of target sequences in the cellular RNA or nucleic acid to the array probes. Regarding claims 228 and 230, Lockhart et al. teach "The target polynucleotide whose sequence is to be determined can be isolated from a clone, a cDNA, genomic DNA, RNA, cultured cells, or a tissue sample"; and further teaches "If the target is mRNA, the sample is obtained from a tissue in which the mRNA is expressed" and "sufficient DNA is present in the tissue sample to dispense with the amplification step", in other words the total

Art Unit: 1637

cellular DNA, which is nucleic acid, is used (see column 21 lines 8-37 and entire reference).

Regarding claim 229, Lockhart et al. teach "The target can be labeled at one or more nucleotides during or after amplification" (see column 21 lines 33-34).

Regarding claim 231, Lockhart et al. teach an array with at least 10,000 different probes by teaching high density arrays of different probes, with probe density ranging from 625 to 10 million probes per 1 cm<sup>2</sup>. (Fig. 2; col. 6, lines 62-67; col. 7).

Regarding claim 232, Lockhart et al. teach the determination of the length of sequence signatures (excludes low information content) and which is the distance between primers/probes (see column 18 lines 42-44). This is a rejection necessitated by amendment.

Regarding claim 122, Lockhart et al. do not specifically teach an array wherein the genomic target sequences for a plurality of probes span a genomic region of at least 25,000 bp.

Bowtell teaches microarrays having regions of 42,000 (42k) and 30,000 (30k) gene sets, each of which is over 25,000 bp and that the entire genome of *C. elegans* (entire reference, especially Table 3, 2<sup>nd</sup> column first two entries, p. 26 column 2 - 2<sup>nd</sup> paragraph, and supporting document, Human Genome Project, p. 3 chart showing 3 billion base for the human genome and 97 million bases for *C. elegans* genome).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al. by spanning genomes as suggested by Bowtell with a reasonable expectation of success. The

Art Unit: 1637

motivation to do so is provided by Bowtell who teach the usefulness of array to span genomes and the teaching of Lockhart et al. that array can span gene families (see Figure 3 and its description in column 5 lines 27-33). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

15. Claim 223 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (US Patent No. 6,329,140 filed 1997) and Bowtell (1999) as applied to claims 122 and 185 above, and further in view of Schena et al. (1996).

Lockhart et al. and Bowtell teach as noted above.

Lockhart et al. and Bowtell do not teach wherein the organism is a plant.

Schena et al. teach microarrays to measure expression of plant genes (see 2<sup>nd</sup> paragraph of p. 10614).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al. and Bowtell by targeting nucleotide sequences of plant genes as suggested by Schena et al. with a reasonable expectation of success. The motivation to do so is provided by Schena et al. who teach usefulness of microarrays in measuring plant genes and the teaching of Lockhart et al. and Bowtell who teach the usefulness of microarrays. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

**Conclusion**

16. No claim is free of the prior art.
17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples *MS*  
Examiner  
Art Unit 1637  
August 14, 2007

*Kenneth R. Horlick*  
KENNETH R. HORLICK, PH.D.  
PRIMARY EXAMINER

*8/15/07*